

Contract Research Drives China's Pharma Sector

Contract research is both a vehicle for Chinese pharmas to expand their R&D expertise and quality levels, and a bridge for them to enter global markets.

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China's pharmaceutical sector has maintained steady growth over the past few years. Last year, total revenues increased by nearly 26%, moving to \$54.6 billion (437.3 billion RMB).

Changes in the competitive landscape, notably China's entry into the World Trade Organization (WTO) in 2001 and the development of a regulatory system through the establishment of China's State Drug Administration (SDA, now called the SFDA), are fueling the growth of contract manufacturing and contract research. Also driving this growth are the *hai gui*, Chinese nationals who return to China after gaining professional experience in Western biopharmaceutical companies.

"The Chinese authorities have brought pharmaceutical regulations forward 20 years in the past six. That is an impressive feat," said James McClurg, Ph.D., senior vice president and CSO at MDS Pharma Services, a Toronto-based clinical research organization (CRO) with a branch in Beijing.

One critical milestone was reached in September 2003, when the SFDA issued Good Clinical Practice (GCP) standards, which clearly defined CRO and stipulated for the first time that CROs in China could conduct clinical trials on behalf of their clients.

Table 1: Major CROs in China

| MULTINATIONAL CROs | Owner | Location | Service |
|--|---------------------|-------------------|----------------------------|
| Pharmaron (Beijing) Pharm. Tech. | Sino-U.S | Beijing | Organic synthesis, R&D |
| Quintiles Transnational Corp. | U.S. | Beijing, Shanghai | Clinical study, regulatory |
| MDS Pharma Services | U.S. | Beijing | Clinical study |
| Beijing KendleWit Medical Consulting Co. | Sino-U.S | Beijing | Clinical study, regulatory |
| Shanghai InCROM Pharma Dev. Co. | Japan | Shanghai | Clinical study |
| CCBR | Denmark | Beijing | Clinical study |
| Bridge Pharmaceuticals | U.S. | Beijing | Animal experiment |
| VenturePharm CRO Service | Sino-U.S- Canada | Beijing | Clinical study |
| Beijing Oriental Xianduan Pharma Tech | Japan | Beijing | Clinical study |

Source: BioPlan Associates, Inc.

| CHINESE CROs | Owner | Location | Service |
|-------------------------------|---------|---------------------|-------------------|
| Wuxi Pharma Tech | Chinese | Shanghai Pudong | Drug R&D |
| Shanghai Genomics Inc. | Chinese | Shanghai Zhangjiang | Drug & gene R&D |
| Shanghai LeadDiscovery Pharma | Chinese | Shanghai Zhangjiang | Drug R&D |
| 2Y-Chem, Ltd. | Chinese | Shanghai Zhangjiang | Drug R&D |
| Zensun Sci &Tech Co., Ltd. | Chinese | Shanghai Zhangjiang | Drug R&D |
| Shanghai Hua Xin Biotech Inc. | Chinese | Shanghai Zhangjiang | Biotech R&D, mfg. |

| | | | |
|--|---------|---------------------|---------------------------------|
| Shanghai GenMed Ltd. | Chinese | Shanghai Zhangjiang | Gene R&D |
| Shanghai IgCon Therapeutics Inc. | Chinese | Shanghai Zhangjiang | Monoclonal R&D |
| Shanghai ChemPartner Co. Ltd. | Chinese | Shanghai Zhangjiang | Drug R&D |
| Shanghai Pharma-pro Service Co. | Chinese | Shanghai Zhangjiang | Drug R&D |
| Shanghai Allist Pharmaceutical | Chinese | Shanghai Zhangjiang | Drug R&D |
| Shanghai Pharma Engine (CRO) Co. | Chinese | Shanghai Zhangjiang | Regulatory, clinical trial |
| Shanghai Res. Center for Biomodel Organism | Chinese | Shanghai Zhangjiang | Gene tech |
| Shanghai Newsummit Biopharma Institute | Chinese | Shanghai Xuhui | Drug R&D |
| Shanghai SLG CRO Co., Ltd | Chinese | Shanghai | Clinical study, regulatory |
| Beijing Huaxi United Tech Dev. Co. Ltd. | Chinese | Beijing | R&D, clinical study, regulatory |
| Giant Med-Pharma Services, Inc. | Chinese | Beijing | Clinical study, regulatory |
| Vector Gene Technology Co., Ltd. | Chinese | Beijing | Gene vector R&D |
| Excel PharmaStudies Inc. | Chinese | Beijing | Clinical study, regulatory |
| Nanjing Chemzam Pharm Tech Co. | Chinese | Nanjing | R&D, regulatory |
| Guangzhou Pudu Pharma Sci. & Tech. Dev. | Chinese | Guangzhou | Drug R&D |
| Guangzhou Boji Clinical Research Center | Chinese | Guangzhou | Clinical study |

Source: BioPlan Associates, Inc.

Growth within China's CRO sector, in turn, is driving the development of the nation's pharmaceutical industry, and enhancing opportunities for international collaboration. "China ... today accounts for a small part of the value of the pharmaceutical and biotechnology industries relative to its huge population," said Dennis Gillings, CEO of Quintiles Transnational at the Boao Forum for Asia's World Pharmaceutical Industry Conference in Taizhou. "But its share of the pharmaceutical market value will grow many times by 2030," he predicted.

Driving that growth will be CROs. This article will examine the growth of CROs in China, and point out emerging trends in the nation's CRO sector.

Since the early 1990s, more and more Chinese Contract Manufacturing Organizations (CMOs) have engaged in Active Pharmaceutical Ingredient (API) production, and many are endeavoring to meet international production standards for finished drugs. In 2004, Chinese CMOs generated \$7.5 billion (RMB 60 billion) in domestic output, accounting for 13% of the country's gross pharmaceutical output — not an insignificant figure given that contract manufacturing is still young in China.

CROs emerged in China in the mid-1990s, when several of the world's leading CROs established a presence in Beijing. Contract research has experienced explosive growth since then, and today China is home to more than 300 CROs of all sizes. This growth has been fueled by demographic changes and economic trends, as well as recognition of the opportunities associated with a market whose potential has been estimated at up to \$1 billion (8 billion RMB).

Contract Research in China



Currently, the U.S. and Europe dominate contract research, with 88% of a \$16.3 billion global market that grew by 14% last year. China's CRO market is very small by comparison right now, accounting for \$62.6 million (RMB 500 million) in 2004, but significant growth is expected as the average costs for developing a new drug continue to rise. The cost of drug development in China is 20% of that of in the U.S. and many other countries.

China's pharma sector faces both challenges and opportunities (*listed in Table 2; click the Download Now button at the end of this article to access a 2-page PDF containing Tables 1 and 2*), but the establishment of Good Clinical Practices (GCP) and China's entry into the WTO, plus the government's pledge to increase IP protection, promise to continue its growth trend.

In 1996, MDS Pharma Services became the first foreign-based CRO to operate in China, focusing on clinical laboratory functions, Phase III multi-center trials and site management. Following that, other

leading CROs — such as Quintiles Transnational, Covance and Kendles — also entered the Chinese market. At this point, only MDS's and Quintiles' Beijing labs have obtained accreditation from the College of American Pathologists (CAP).

Meanwhile, a growing number of global pharma companies including Novo Nordisk, AstraZeneca, Eli Lilly, Roche and Pfizer, have established or plan to establish R&D centers in China. Each is looking for Chinese CRO partners; so are domestic Chinese pharma companies.

Even as Chinese pharmas have made GMP modifications, 45% of their production facilities are idle, presenting a significant financial challenge. As a result of this excess capacity, Chinese pharmas are essentially operating under a CMO model, and some are aggressively seeking contract manufacturing opportunities overseas to keep their facilities running.

Currently, 259 products associated with 130 Chinese manufacturers have obtained cGMP certification from the U.S. Food and Drug Administration (FDA), and 50 manufacturers have obtained 90 European COS certificates. Among them, 10 finished drug manufacturers have received cGMP certification from FDA.

China's more than 300 CROs form an integrated service chain, addressing everything from pharmacogenomics to clinical trials, new drug applications, new drug transfers and exporting. The majority of Chinese CROs are small and simply provide regulatory consultation, drug application and clinical trial assistance to overseas pharma firms. Of these, more than 100 are capable of conducting R&D.

Major Chinese CROs are located primarily in Shanghai and Beijing, especially in two large biotech parks: Shanghai Zhangjiang Biopharmaceutical Park (part of the Zhangjiang Hi-tech Park) and Beijing Zhonguancun Life Science Park (*see Table 1*).

Beijing alone boasts more than 100 CROs. China also has upwards of 1,000 domestic research institutions associated with biotech and pharmaceutical science. Besides CROs, numerous research institutes supported by the Chinese government or by drug companies are open to contract research opportunities.

For example, Tianjin Pharmaceutical Institute specializes in drug metabolism studies; Shanghai Pharmaceutical Industry Institute specializes in toxicology studies, and Shanghai Institute of Materia Medica (affiliated with the Chinese Academy of Science) has been collaborating with GlaxoSmithKline on the development of a chemical compound database since early 2005.

So far, 15 laboratories in China have received SFDA-issued GLP certifications; eight more laboratories have passed the GLP examination and are waiting to receive the certification. It is estimated that 30 laboratories will be GLP-certified by the end of 2006.

Shanghai Focuses on Drug Development



On Feb. 22, 2005, Shanghai Biopharmaceutical R&D CRO Service Base and Shanghai Pudong Biopharmaceutical R&D CRO Service Center formally opened in the Shanghai Zhangjiang Hi-tech Park. The Center, which plans to become Asia's largest CRO facility, will operate under U.S. GLP standards. It projects annual revenue in excess of \$250 million (2 billion RMB) — 10 times its current level. The Center plans to attract over 5 billion RMB (U.S. \$625 million) in biotech investment from within and outside China in the next five years. "So far, 29 Chinese CROs have settled in our center and more companies are preparing to join us over time," said Hui Lin, associate director general.

Shanghai Genomics, Inc. is one company that has joined the Center. "Participating in global drug research and development improves our capability to innovate," said Dr. Ying Luo, president and CEO. "As [more] Chinese CROs obtain overseas research contracts, they'll be able to keep pace with worldwide pharmaceutical R&D, advance technology frontiers and establish standards for managing and operating R&D facilities."

Dr. Luo's company obtained a contract research project from Johnson & Johnson concerning cancer-related gene clones in Feb. 2005, and signed a two-year collaboration pact with Dutch biopharma firm

Organon in Jan. 2006 for research involving identification of a more selective steroid hormone receptor modulator.

Dr. Ge Li, president of Wuxi Pharma Tech, China's largest pharma CRO, is very optimistic about the contract research industry in China. "In the next few years, we hope our company will continue growing by more than 50% annually," he said. Since he established his firm in 2001, it has become China's largest pharmaceutical R&D service firm and the world's fastest growing pharma services company. Within three years, its revenues expanded nearly seven-fold, reaching \$21 million in 2004. The firm has 70 clients around the world, including 26 of the world's top biopharma and pharma companies, and has been profiled as a case study by Harvard Business School.

Since the first global CROs set up shop in Beijing, a growing number of Western CROs have joined them to build clinical research bases and animal experimental centers. Within the past three years, 29 biopharma projects worth \$450 million (RMB 3.6 billion) have been located in the capital, according to Ting Lei, director of the Beijing Pharma and Biotech Center. Says MDS's McClurg, "As China improves its regulatory structure, the environment will become more normalized and more reliable. People there are recognizing the importance of playing by the regulatory and business rules [of other countries]."

McClurg believes that more people will begin to consider Chinese firms as potential partners. "However, it would be a mistake to go there with the primary reason of saving money," he cautions. "The decision should be made based on the importance of the domestic opportunity. Your expense profile will be different, but not substantially less. Reduced personnel costs will be offset by increased real estate costs, increased travel, management, training, and start-up time and expenses. Establishing personnel policies and finding the right partners is a long-term process that takes a real commitment."

In short, the next 10 years will be an important period for the expansion of contract research in China. Chinese CROs will facilitate the development of China's international pharmaceutical and biopharmaceutical industries.

Table 2: Advantages and Disadvantages of China's Pharma Segment

Advantages

- Low cost of drug development
- Large domestic market potential
- Rich clinical/disease resources
- Plentiful, trained human resources
- Government support
- Rapidly evolving market environment
- Increasingly innovative drug R&D
- Growing government commitment to IP protection
- Plentiful R&D institutions

Disadvantages

- Lack of domestic funding resources and venture capital
- Overall R&D level is comparatively low
- Insufficient communication platform
- Lack of experience in regulatory and other specialized areas
- Laboratory facilities tend to be less advanced
- Most CROs are small
- Evolving financial structures
- IP protection issues not fully resolved

About the Author

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Bibliography

Shuguang, B., *Prospect of pharmaceutical industry [in Chinese]*, *Securities Times*. 2001, June 9

China Pharmaceutical Industry Development Report 2003 [in Chinese]. 2003, June [online]. Available from <http://report.cei.gov.cn/hy/yy.htm> SFDA Southern Medicine Economic Institute *Pharmaceutical Economic data 2003 -2005 [in Chinese]*

Statistics released by the SFDA Southern Medicine Economic Institute [in Chinese], 2006, April 10

Haiying, Y. *Analysis of overseas pharmaceutical OEMs [in Chinese]*. *China Drug Store* 2006, 1: 40-43

Yimin, C., *Chinese CROs: Moving forward with persistence [in Chinese]*. *Medicine Economy News* 2005, Mar. 7

Speech excerpt of Boao Forum for Asia's World Pharmaceutical Industry Conference. *Taizhou News* 2006, Apr.28

Lu. M. *CROs help new drug R&D [in Chinese]*. *Medical World* 2005, 6: 56-57
SFDA, Good Clinical Practice (GCP) [in Chinese]. 2003, Sep. 1

China Pharmaceutical Enterprise Management Association Survey, 2005

Zongpin, L., *China's labor cost is 1/10 of that of U.S.—Pharmaceutical outsourcing is warming up [in Chinese]*. *Beijing News* 2006, May 5

Hui, X., *CROs and pharmaceutical parks in China [in Chinese]*. *Shanghai Medical and Pharmaceutical Journal* 2004,27 (1): 12-13

Na., L., *Wuxi Pharma Tech expands the pharmaceutical R&D CRO business [in Chinese]*. *IT Manager World* 2005, 12: 76